REMARKS

The present response is intended to be fully responsive to all points of objection and/or rejection raised by the Examiner and is believed to place the application in condition for allowance. Favorable reconsideration and allowance of the application is respectfully requested.

Claims 70, and 80-81 are pending. Claim 70 has been amended. Claim 81 has been canceled. Claims 1-69, 71-79 and 82-89 are held withdrawn. The support for the amended claim 70 is found in paragraphs [0196], [0207] and [0209].

Applicants respectfully assert that the amendments to the claim add no new matter. Applicants request the Examiner to enter the amendment.

35 U.S.C. § 103 Rejections

In the Office Action, the Examiner rejected claims 70, 80 and 81 under 35 U.S.C. § 103(a), as being allegedly unpatentable over the combined teaching of Yedgar et al. and Chaikof et al. in view of Sorgente et al.

The Examiner asserted that Yedgar et al. is directed to anti-inflammatory derivatives including distearoyl phosphatidylethanolamine covalently bonded through the amine group to carrier moieties which may include polysaccharides. The Examiner admitted that the instant invention differs from the teaching of Yedgar et al. in that chondroitin sulfate is not specifically mentioned as a carrier moiety. The Examiner further asserts that Yedgar et al. do not intend their listing to be exhaustive and chondroitin sulfate is a polysaccharide.

The Examiner asserted that Chaikof et al. discloses targeting of therapeutic agents using glycophospholipids generically overlapping applicants'. The Examiner further asserted that Chaikof et al. disclose the saccharide derivative used in the glycophospholipid may itself be therapeutic and specifically mentioned chondroitin sulfate. The Examiner admitted that Chaikof et al. does not specifically mention the utility of chondroitin sulfate. The Examiner asserted that Sorgente et al. discloses chondroitin sulfate to be useful as an anti-inflammatory. The Examiner asserted that it would have been allegedly prima facie obvious at the time the

invention was made to start with the teaching of the cited references, to make applicants' compounds and to expect to produce anti-inflammatory agents.

In response, Applicants traverse the Examiner rejection of Claims 70, 80 and 81 under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combined teachings of Yedgar et al. and Chaikof et al. in view of Sorgente et al.

Applicants assert that it would not have been obvious to one skilled in the art to prepare an intact GAG compound, such as chondroitin sulfate, covalently conjugated via an amide bond to phosphatidylethanolamine to obtain a compound having preferred therapeutic properties as discussed below. Moreover, the Examiner has not provided any motivation as to why one skilled in the art would prepare same.

Yedgar et al., Chaikof et al. and Sorgente et al., alone or in combination, do not teach or suggest a compound wherein chondroitin sulfate is covalently bound to phosphatidylethanolamine via an amide bond. Yedgar et al discloses phosphatidylethanolamine covalently bound to an inert carrier, which carrier inhibits cell internalization of the cell-permeable PLA_2-inhibitor moiety. Moreover, the Examiner admitted that chondroitin sulfate is not specifically mentioned as a carrier moiety in Yedgar et al, and further, since chondroitin sulfate, a glycosaminoglycan (GAG) which plays a key role in protecting cells from diverse damaging agents and processes, Yedgar et al does not render obvious the conjugation of the two, which provides superior therapeutic effect (page 6, paragraph [0116]). Applicants unexpected results clearly show that GAG-lipid conjugates (such as chondroitin sulfate - phosphatidylethanolamine conjugate and hyaluronic acid - phosphatidylethanolamine conjugate) have greater therapeutic effect as compared to non-GAG lipid conjugates, and less toxicity.

The Examiner has admitted that Chaikof et al. does not teach a utility for chondroitin sulfate as a therapeutic agent, moreover, Chaikof et al. do not disclose a biodegradable conjugate, rather in Chaikof et al. the saccharide is linked to the phospholipid via non-biodegradable ether bonds. Accordingly, Chaikof et al. did not render obvious a chondroitin sulfate - phosphatidylethanolamine biodegradable compound, with therapeutic activity. Applicants, however, provide phospholipids covalently bound to a chondroitin sulfate via an amide bond (page 13, paragraph [0209]), which is biodegradable and contributes to the

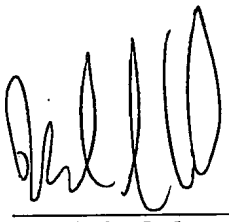
therapeutic effect of the GAG. Unexpected results by the Applicants show that biodegradable lipid conjugates possess greater therapeutic effect than non- biodegradable lipid conjugates, negligible toxicity, and superior anchoring of the GAG to the cell surface via multiple phospholipids conjugated to the GAGs, enriching the cell surface with GAGs. Therefore, combining Yedgar and Chaikof does not render obvious to one skilled in the art a GAG compound, such as chondroitin sulfate, covalently conjugated via a biodegradable amide bond to a multiplicity (n) of phosphatidylethanolamine residues, and the therapeutic effect exerted specifically by such a conjugation.

Sorgente et al. describes methods and compositions for the treatment of conditions related to cartilage degradation or inflammation. Chondroitin sulfate is disclosed as a participatory agent useful in the treatment of such conditions when administered in a composition containing collagen. No conjugation of chondroitin sulfate is taught by Sorgente. Applicants demonstrate therapeutic effects mediated via the covalent conjugation of phosphatidylethanolamine to chondroitin sulfate, via amide linkage. Applicants unexpectedly discovered a superior therapeutic effect as a result of the specific conjugation, unparalleled in the administration of individual components (page 7, paragraph [0123]), where non-conjugated GAGs were considerably less therapeutic than conjugated GAGs, (see Fig. 3).

Combining Sorgente with Yedgar, Chaikof, or both, therefore, does not teach the therapeutic activity of a chondroitin sulfate - phosphatidylethanolamine conjugate, via a biodegradable amide linkage, and does not render obvious such a conjugate, neither in terms of the superior activity nor in terms of negligible toxicity discovered by Applicants. Accordingly, Applicants assert that it would not have been obvious to one skilled in the art to combine the teachings of Yedgar et al., Chaikof et al. and Sorgente et al., and to covalently conjugate chondroitin sulfate to phosphatidylethanolamine, via an amide bond to obtain a compound having preferred therapeutic properties as discussed above. Therefore, Yedgar et al., Chaikof et al. and Sorgente et al., alone or in combination, do not teach or suggest the invention of claims 70, 80 and 81.

No fee is deemed necessary for filing this Amendment. However, if any fee is required, the undersigned Attorney hereby authorizes the United States Patent and Trademark Office to charge Deposit Account 05-0649.

Respectfully submitted,



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